

## REMARKS

The present Reply is accompanied by a Petition for three one-month extensions of time, and by a Request for Continued Examination.

By the present Reply, no claims have been added, canceled, or amended. Accordingly, claims 1-13 are under prosecution, and favorable reconsideration thereof is respectfully requested. Claim 1 is the independent claim.

### 35 U.S.C. 103 (a)

#### **Branton in view of Aich**

The Examiner has expressed the view that claims 1-3 and 5-13 are unpatentable under 35 U.S.C. 103(a) over United States Patent No. 6,627,067 to Branton *et al.* ("Branton") in view of PCT Publication No. WO 99/31115 to Aich *et al.* ("Aich").

Applicant respectfully submits that the cited references fail to satisfy the requirements for a finding of obviousness of the independent claim. In the submissions presented below, Applicant has first addressed the *Graham v. John Deere* factual inquiries, to assist the Examiner in understanding the factual basis for the Applicants' position. Applicants have then addressed the non-obviousness of the pending claims, specifically addressing the various points raised by the Examiner in the present Office Action.

In *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 at 17-18 (1966), the Supreme Court set out the following objective framework for applying the statutory language of §103:

"Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."

Thus, the factual inquiries enunciated by the Court in Graham are as follows:

- (1) Determining the scope and content of the prior art;
- (2) Ascertaining the differences between the claimed invention and the prior art; and
- (3) Resolving the level of ordinary skill in the pertinent art.

#### 1) Scope and Content of the Prior Art

The Examiner has cited two references in respect of the present rejection. First, the Examiner relies on Branton, which discloses a method for evaluating a polymer molecule (Abstract). Some of the embodiments disclosed in Branton include a detector capable of detecting polymer molecule characteristics (column 5 lines 31-32), and in some embodiments, a polymer molecule traverses an aperture by application of a voltage (column 6 lines 7-8).

With respect to claim 1, the Examiner has referred particularly to passages in column 20 of Branton, namely at lines 20-21, 37-41, and 57-58. This portion of Branton discusses separation of double-stranded DNA (line 23, for example), and translocation rates of single-stranded polynucleotides and double-stranded or hybridized polynucleotides at various voltage gradients. For example, Branton discloses obtaining a hybridized polynucleotide, and pulling the double-stranded polynucleotide through a channel under a given voltage gradient (lines 37-41).

Significantly, Branton appears to be directed to a method for evaluating a polymer molecule, and does not appear to contemplate recording information in a nucleic acid polymer, for example. More particularly, as the Examiner indicated (Office Action page 4), Branton is silent about incorporation of a metal ion in a nucleic acid duplex, and Branton does not appear to discuss metal ions at all. And while Branton does disclose obtaining a hybridized polynucleotide (column 20 line 38, for example), Branton does not appear to provide any discussion or recognition whatsoever of any kind of modulation as a duplex forms in a hybridization medium.

Aich discloses, in one illustrative embodiment, methods for making conductive metal-containing nucleic acid duplexes, comprising subjecting a nucleic acid

duplex to basic conditions in the presence of a divalent metal cation (Abstract). However, Aich does not appear to contemplate modulating the translocation of first and second nucleic acid strands through a channel, nor does Aich appear to contemplate modulating an electrostatic potential across the channel, for example.

2) Differences between the claimed invention and the cited references

Independent claim 1, as previously amended, recites:

1. A process of recording information in a nucleic acid polymer, comprising:
  - a) modulating the translocation of first and second nucleic acid strands through a channel between a dissociation medium and a hybridization medium, while modulating an electrostatic potential across the channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms in the hybridization medium, so that if a metal ion is permitted to enter the duplex a metal-containing base pair is formed and if a metal ion is excluded from the duplex a non-metal-containing base pair is formed;
  - b) wherein the channel separating the hybridization medium and the dissociation medium is dimensioned to allow linear translocation of the nucleic acid duplex or a metal-containing nucleic acid duplex between the hybridization medium and the dissociation medium;
  - c) and wherein the first and the second nucleic acid strands comprise a plurality of nitrogen-containing aromatic bases covalently linked by a backbone, the nitrogen-containing aromatic bases of the first nucleic acid strand being capable of being joined by hydrogen bonding in the hybridization medium to the nitrogen-containing aromatic bases of the second nucleic acid strand so that the nitrogen-containing aromatic bases on the first and the second nucleic acid strands form hydrogen-bonded base pairs in stacked arrangement in the nucleic acid duplex, the hydrogen-bonded base pairs being capable of

interchelating the metal cation coordinated to a nitrogen atom in one of the aromatic nitrogen-containing aromatic bases to form the metal-containing nucleic acid duplex.

It is submitted that neither of the cited references discloses or suggests modulating an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, as recited in claim 1. It is submitted that this and other important differences between the cited references and the subject matter of claim 1 weigh heavily in favour of the non-obviousness of claim 1.

Although Branton appears to disclose varying a voltage gradient that pulls a polynucleotide through a channel (column 20 lines 33-41, and column 21 lines 16-24, for example), Applicant respectfully submits that this disclosure falls far short of offering any apparent reason for modulating an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, as recited in claim 1. Varying a voltage that moves a polynucleotide through a channel is significantly different, in principle and in practice, from modulating incorporation of a metal ion in a duplex as the duplex forms, as recited in claim 1. As disclosed in Branton, variations in the voltage gradient may be appropriate for single-versus double-stranded polynucleotides (column 20 lines 33-41), or to facilitate monitoring an effect of an individual monomer on ionic or electronic current (column 21 lines 43-50), for example. However, it is submitted that Branton simply does not contemplate incorporation of a metal ion in a nucleic acid duplex, and offers no discussion or recognition whatsoever that modulating an electrostatic potential across a channel may have this advantage.

Furthermore, it is submitted that the variations in voltage gradient disclosed by Branton do not appear to take place as a duplex forms, and therefore the disclosure of Branton is largely unrelated to the modulating of an electrostatic potential recited in claim 1.

In summary, it is submitted that Branton discloses no apparent reason for modulating an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms.

As indicated above, it is submitted that there are numerous significant differences between Aich and the subject matter of claim 1. For example, the cited Aich reference does not appear to contemplate any modulation of electrostatic potential, nor does the reference appear to contemplate translocation of first and second nucleic acid strands through a channel, for example.

In summary, it is submitted that neither of the cited references, alone or in combination, offers any apparent reason whatsoever for modulating an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, as recited in claim 1. This important difference between claim 1 and the cited references strongly suggests that claim 1 is not obvious in view of those references.

### 3) The level of ordinary skill in the pertinent art

Applicant respectfully requests the Examiner to consider carefully the knowledge that the notional person of ordinary skill in the art would have possessed, and more importantly, the knowledge that one of ordinary skill in the art would not have possessed, at the time the present invention was made.

Having regard to the cited references, it is submitted that one of ordinary skill in the art would have understood from the Aich reference that subjecting a nucleic acid duplex to basic conditions in the presence of a divalent metal cation could make conductive metal-containing nucleic acid duplexes, for example. Also, a person of ordinary skill in the art would have known from the Branton reference that a voltage gradient can pull a polynucleotide through a channel (column 20 lines 23-52), and that voltages could be varied to advance a DNA molecule stepwise through a channel (column 21 lines 43-50), for example.

However, it is submitted that having regard to the cited references, the notional person of ordinary skill in the art would not have had any reason to modulate an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, as recited in claim 1.

Moreover, it is submitted that the notional person of ordinary skill in the art would not turn to the cited references to determine how to record information in a nucleic acid polymer. In particular, the Branton reference discloses a method for evaluating a polymer molecule (Abstract), and does not appear to include any discussion regarding metal ions, or to be directed in any way to methods of recording information in a nucleic acid polymer. Branton is directed to a significantly different application, and therefore, it is submitted that the notional person of ordinary skill in the art, pursuing methods of recording information in a nucleic acid polymer, would not even consider the Branton reference to be relevant, and would perceive no reason to combine the Branton reference with any other art.

In summary, it is submitted that one of ordinary skill in the art, on reading the cited references, would not perceive any apparent reason to modulate an electrostatic potential across a channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, and that incorporation of metal ions in the manner of claim 1 would be an unexpected result to the notional person, having reviewed the cited references.

#### Discussion of non-obviousness

As discussed above, important differences exist between the cited references and the claimed invention. These differences provide significant advantages, by forming metal-containing base pairs and non-metal-containing base pairs to record information in a nucleic acid polymer, for example. The cited references do not appear to recognize any such advantage of modulating an electrostatic potential in the manner recited in claim 1, and simply would not lead the notional person of ordinary skill to the invention of claim 1.

Applicant respectfully submits that for at least these reasons, all three of the *Graham* factual inquiries weigh in favour of the non-obviousness of claim 1.

With respect to the second *Graham* factual inquiry, the differences between claim 1 and the cited references provide a significant advantage, by permitting information to be recorded in a nucleic acid polymer. With respect to the third *Graham* factual inquiry, the notional person of ordinary skill in the art would not have perceived any apparent reason to modify or combine the cited references, nor would the notional person of ordinary skill in the art perceive any reason to modulate an electrostatic potential in the manner recited in claim 1.

In summary, the *Graham* factual inquiries favor a finding of non-obviousness of claim 1. Applicant therefore respectfully submits that the cited references fail to satisfy the requirements for a finding of obviousness of claim 1, and respectfully requests that the rejection of claim 1 under 35 U.S.C. 103(a) be withdrawn.

Claims 2-13 depend directly or indirectly from independent claim 1. Accordingly, Applicant respectfully submits that these claims are not obvious in view of the cited references due to their dependencies, and due to the additional subject matter that these claims recite. Applicant therefore respectfully requests that the rejection of claims 2-13 under 35 U.S.C.103 (a) be withdrawn.

**Branton in view of Aich and in further view of Anazawa**

The Examiner has expressed the view that claims 1 and 4 are unpatentable under 35 U.S.C. 103(a) over Branton and Aich in further view of United States Patent No. 6,136,543 to Anazawa *et al.* ("Anazawa").

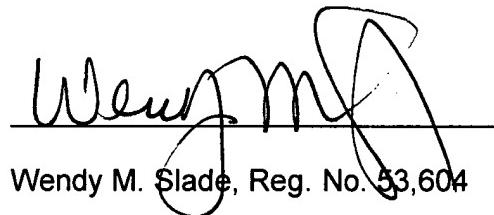
Anazawa discloses a single molecule of single-stranded sample DNA having a bead at one end and a magnetic bead at the other end (Abstract). However, it is submitted that Anazawa also fails to disclose or suggest modulating an electrostatic potential across the channel so as to modulate the incorporation of a metal ion in a nucleic acid duplex as the duplex forms, as recited in claim 1. Accordingly, it is submitted that Branton, Aich, and Anazawa, alone or in combination, fail to disclose this feature of claim 1. Therefore, it is submitted that the cited references fail to satisfy the requirements for a finding of

obviousness of claim 1, and Applicant respectfully requests that the rejection of claim 1 under 35 U.S.C. 103(a) be withdrawn.

Claim 4 depends directly from claim 1, and Applicant respectfully submits that the cited references fail to satisfy the requirements for an obviousness rejection of claim 4 due to its dependency, and due to the additional subject matter that this claim recites. Therefore, Applicant respectfully requests that the rejection of claim 4 under 35 U.S.C. 103(a) be withdrawn.

In view of the foregoing, Applicant respectfully submits that the present application is in condition for allowance, and respectfully requests that a Notice of Allowance be issued. Should the Examiner have any further concerns, the Examiner is respectfully invited to contact the undersigned agent at the telephone number appearing below, to expedite further prosecution on allowance of this application.

Respectfully submitted,



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